

**AMENDMENTS TO THE CLAIMS:**

*Please amend claims as set forth below.*

- 1-34. (Canceled).
35. (Currently amended) A transgenic mouse comprising in its genome a yeast artificial chromosome (YAC), wherein the YAC contains at least a majority of the human Ig V $\lambda$  genes of cluster A and all the human Ig J $\lambda$ - C $\lambda$  segments in germline configuration, wherein the proportion of the  $\kappa$  and  $\lambda$  light chains expressed by said transgenic mouse resembles that found in humans, and exhibits relative proportions of <60%  $\kappa$  light chains and >40%  $\lambda$  light chains, wherein at least one endogenous  $\kappa$  light chain locus of the transgenic mouse is not disrupted.
36. (Previously presented) The transgenic mouse according to claim 35, wherein the YAC is about 410 Kb, and wherein the YAC containing human Ig segments shows high expression and is able to compete with the endogenous mouse  $\kappa$  locus.
37. (Previously presented) The transgenic mouse according to claim 35, wherein one of the endogenous Ig $\kappa$  loci of the mouse is disrupted, and wherein the YAC containing human Ig segments shows high expression.
38. (Previously presented) The transgenic mouse according to claim 35, comprising a 380 Kb region of the human immunoglobulin (Ig)  $\lambda$  light (L) chain locus in germline configuration, wherein the 380 Kb region resides on a yeast artificial chromosome (YAC) that accommodates the most proximal V (variable gene)  $\lambda$  cluster, wherein the 380 Kb region has 15 V $\lambda$  genes and all J $\lambda$ - C $\lambda$  segments with the 3' region, wherein the 3' region includes a downstream enhancer.

39. (Previously presented) The transgenic mouse according to claim 35, wherein the mouse includes a Hulg $\lambda$  YAC that accommodates a 380 Kb region of the human  $\lambda$  light chain locus in authentic configuration with all V $\lambda$  genes of cluster A, the J $\lambda$ - C $\lambda$  segments and the 3' enhancer.
40. (Previously presented) The transgenic mouse according to claim 39, wherein the Hulg $\lambda$  YAC is shown in Figure 1.
41. (Previously presented) A method for producing a transgenic mouse according to claim 35, comprising:
  - (a) introducing a Hulg $\lambda$  YAC into murine embryonic stem cells, wherein the Hulg $\lambda$  YAC accommodates a 380 Kb region of the human  $\lambda$  light chain locus in germline configuration with all V $\lambda$  genes of cluster A, the J $\lambda$ - C $\lambda$  segments, and a downstream enhancer at the 3' region; and
  - (b) deriving a transgenic mouse from the cells of step (a) by blastocyte injection to form a chimeric animal and then breeding the chimeric mouse to obtain a transgenic mouse.
42. (Previously presented) The method of claim 41, wherein the Hulg $\lambda$  YAC is about 410Kb.
43. (Previously presented) The method according to claim 41, wherein two copies of the neomycin resistance gene (NEO $^r$ ) are site-specifically integrated into the ampicillin gene on the left (centromeric) YAC arm in order to permit selection.
44. (Previously presented) The method according to claim 41, wherein YAC-containing yeast cells are fused with HM-1 embryonic stem (ES) cells and G418 resistance colonies are picked and analysed 2-3 weeks after protoplast fusion.

45. (Previously presented) The method according to claim 41, wherein ES cells containing a complete Hulg $\lambda$  YAC copy are used for blastocyte injection to produce a chimeric animal.
46. (Previously presented) The method according to claim 45, wherein breeding of a chimeric animal with a Balb/c mouse results in germline transmission.
47. (Currently amended) The method according to claim 46, wherein the germline transmission comprising breeding the mouse with  $\kappa^+$  mice to establishes lines of transgenic mice, wherein at least one endogenous  $\kappa$  light chain locus of the transgenic mouse is not disrupted.
48. (Currently amended) A transgenic mouse comprising in its genome a yeast artificial chromosome (YAC), wherein the YAC contains at least a majority of the human Ig V $\lambda$  genes of cluster A and all the human Ig J $\lambda$ - C $\lambda$  segments in germline configuration, and expressing human  $\lambda$  light chain locus genes and endogenous  $\kappa$  light chain locus genes, wherein the expression of the human  $\lambda$  locus is equal to or greater than that of the endogenous  $\kappa$  light chain locus, and wherein at least one endogenous  $\kappa$  light chain locus of the transgenic mouse is not disrupted.
49. (Previously presented) The transgenic mouse according to claim 48, wherein the mouse further comprises a human  $\kappa$  light chain locus and wherein expression of the human  $\lambda$  light chain locus is equal to or greater than that of the human  $\kappa$  light chain locus.
- 50 (Previously presented) The transgenic mouse according to claim 48, wherein the  $\lambda$  locus has been bred to homozygosity.

51. (Previously presented) The transgenic mouse according to claim 48, wherein the rearranged variable genes in the  $\lambda$  locus are subject to somatic hypermutation.
52. (Currently amended) The transgenic mouse according to claim 48, wherein the mouse comprises a yeast artificial chromosome (YAC) of greater than 100Kb which contains ~~a proportion at least a majority~~ of the human  $V\lambda$  genes proximal to the  $J\lambda$ - $C\lambda$  cluster in germline configuration.
53. (Previously presented) The transgenic mouse according to claim 52, wherein the YAC includes a 380 Kb region of the human  $Ig\lambda$  locus in authentic configuration with at least a majority of the  $V\lambda$  genes of cluster A,  $J\lambda$ - $C\lambda$  segments and a 3' enhancer.
54. (Previously presented) The transgenic mouse according to claim 52, wherein the transgenic mouse comprises variable, joining and constant genes of the human  $\lambda$  light chain locus as a transgenic locus on a YAC, wherein B cells of said mouse rearranges said  $\lambda$  light chain genes and the mouse expresses serum immunoglobulins containing human  $\lambda$  light chains.
55. (Previously presented) The transgenic mouse according to claim 52, wherein the  $\lambda$  locus is rearranged with similar efficiency as endogenous mouse  $\kappa$  and at the same time as or before the endogenous  $\kappa$  locus.
56. (Previously presented) The transgenic mouse according to claim 52, wherein one of the the endogenous  $\kappa$  loci is silenced, and the mouse expresses serum immunoglobulins containing human  $\lambda$  light chains.
57. (Previously presented) The transgenic mouse according to claim 52, further comprising human heavy chain genes as a second transgenic locus integrated

on a separate YAC, wherein the mouse expresses serum immunoglobulin molecules containing combinations of human heavy and  $\lambda$  light chains.

58. (Previously presented) The transgenic mouse according to claim 57, wherein the second transgenic locus carries a diversity of human heavy chain constant region genes and includes  $\mu$ ,  $\delta$  and  $\gamma$  genes.
59. (Previously presented) The transgenic mouse according to claim 58, wherein the heavy chain transgenic locus carries a diversity of human heavy chain constant region genes and includes  $\mu$ ,  $\delta$  and  $\gamma$  genes, wherein the heavy chain constant regions genes are in authentic germline configuration.
60. (Previously presented) The transgenic mouse according to claim 52, further comprising human  $\kappa$  light chain genes as a second transgenic light chain locus integrated on a separate YAC, wherein the mouse expresses serum immunoglobulin molecules containing human  $\kappa$  and  $\lambda$  light chains.
61. (Previously presented) The transgenic mouse according to claim 52, further comprising human heavy chain genes as a second transgenic locus and human  $\kappa$  light chain genes as a third transgenic locus, wherein the mouse expresses serum immunoglobulin molecules containing human heavy chains in combination with at least one of human  $\kappa$  or  $\lambda$  light chains.
62. (Currently amended) The transgenic mouse according to claim 52, wherein expression of the endogenous mouse heavy and/or light chain loci are prevented and the transgenic mouse expresses serum immunoglobulin containing human heavy and/or light chains, wherein at least one endogenous  $\kappa$  light chain locus of the transgenic mouse is not disrupted, and wherein the transgenic mouse is deficient in production of mouse immunoglobulin.